

## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCI United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Vigginia 22313-1450

_	APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
_	09/825,580	04/02/2001	Michael J. Eppihimer	GFN-5398	9952
	7	590 07/28/2003			
	09/825,580 04/02/2001 Michael J. Eppihimer  7590 07/28/2003	EXAMINER			
GARRETT & DUNNER LLP		GAMBEL, PHILLIP			
				,	
	WASHINGTO	N, DC 20005-3315		ART UNIT	PAPER NUMBER
		•		1644	i
				DATE MAILED: 07/28/2003	

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)								
Office Action Summary	09/825580	EPP41min								
	Examiner GAMIDEL	Art Unit								
The MAILING DATE of this communication	THY WAR	1644								
The MAILING DATE of this communication app	ears on the cover sheet with the c	orrespondence address -								
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE MONTHS) FROM  THE MAILING DATE OF THIS COMMUNICATION.  Extensions of time may be evallable under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed  if the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.  If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.  Fallure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any  Status  This action is FINAL.  2b) This action is action is FINAL.										
					3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is Disposition of Claims  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is Disposition of Claims					
					4) Claim(s) is/are pending in the application	4) Claim(s) is/are pending in the application. /-LU L3-LT  4a) Of the above claim(s) is/are withdrawn from consideratio  5) Claim(s) is/are allowed				
					4a) Of the above claim(s) is/are withdraws					
VILI Claim(s) is/are allowed										
7) Claim(s) Is/are rejected. /-1/2 23-27  7) Claim(s) Is/are objected to.  8) Claim(s) are subject to restriction and/or election requirement  Application Papers  9) The specification is objected to by the Examiner.  10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.  Applicant may not request that any objection to the second or by the Examiner.										
					0	If approved, corrected drawings are required in reply to this Occ.				
					If approved, corrected drawings are required in reply to					
					The data of declaration is objected to by the Examin	12) The oath or declaration is objected to by the Examiner.				
					Phorny under 35 U.S.C. §§ 119 and 120	13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).				
					13) Acknowledgment is made of a claim for foreign price					
					a) All b) Some * c) None of:	only under 35 U.S.C. § 119(a)-(d	) or (f).			
1. Certified copies of the priority documents have	/o ha !									
2. Certified copies of the priority documents have	ve been received.									
		lo								
"To ditaction detailed Utilice action for a liet of the	3. Copies of the certified copies of the priority documents have been received in Application No application from the International Bureau (PCT Rule 17.2(a)).  * See the attached detailed Office action for a list of the certified copies not received.  4) Acknowledgment is made at a place of a place of the certified copies not received.									
and the strategy of a claim for domestic price	ribuunda- or u o a									
a) The translation of the foreign language provision	nal application has been	a provisional application).								
Attachment(s)	15) Acknowledgment is made of a claim for domestic priority under this been received.									
1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	4) Interview Summary (PTO	-413) Paner No(s)								
Paper No(s)	Thouse of informal Patent,	Application (PTO-152)								
U.S. Patent and Trademark Office PTO-326 (Rev. 04-01)	6) [_] Other:									
Office Action Su										

MPORNO.17

Part of Paper No.

## **DETAILED ACTION**

 Applicant's amendment, filed 5/28/03 (Paper No. 16), has been entered. Claims 21-22 have been canceled.
 Claims 1, 2, 8, 17, 23 and 25 have been amended.

Claims 1-20 and 23-27 are under consideration.

As pointed out previously upon request, applicant did not distinguish the initial Restriction Groups other than to indicate that there was no serious burden in examining all the claims at once. Given applicant's silence, it has appeared that the claims set forth in initial Restriction Groups II and III recite inherent properties (i.e. "Increasing the movement of cells relative to blood cells" and "inhibiting the effect of thrombus-inducing agents") of "methods of treating or inhibiting thrombosis in a subject comprising administering a composition comprising an effective amount of a P-selectin antagonist" (now PSGL-1) set forth in Group I. Therefore, in the interest of compact prosecution, claims 1-27 (now claims 1-20 and 23-27) employing PSGL-1 as the P-selectin antagonist have been under consideration in the instant application. Applicant has not disagreed with this assessment.

- 2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 5/28/03 (Paper No. 16). The rejections of record can be found in the previous Office Action (Paper No. 14).
- 3. Given applicant's amended claims limiting the claims to the use of PSGL-1 and P-selectin binding fragments thereof, filed 5/28/03 (Paper No. 16), the previous rejection under 35 U.S.C. 112, first paragraph, enablement, has been withdrawn.

Applicant's arguments, filed 5/28/03 (Paper No. 16), concerning enablement are acknowledged, but are not found convincing for the reasons of record. Furthermore, applicant's arguments are rendered moot in view of applicant's amended claims, filed 5/28/03.

4. Claims 1-4, 8-13, 16-18 and 26-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cummings et al. (U.S. patent No. 5,464,778) (see entire document) for the reasons of record set forth in Paper No. 14.

Applicant's arguments, filed 5/28/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submit that Cummings fail to disclose each and every limitations of the claimed invention, as recited in amended independent claims 1, 23 and 25.

Applicant acknowledges that Cummings discloses leukocyte adherence, inflammation, tumor metastases and coagulation and asserts that Cummings speculates on the use of a P-selectin ligand to modulate these conditions (see column 18, lines 34-39).

Applicant asserts that Cummings fails to comment on the role of PSGL-1 in thrombosis nor any teaching of a thrombus-inducing agent including LTC<sub>4</sub>.

Applicant asserts that a certain result or characteristic may occur may occur or be present in the prior art is not sufficient to establish the inherence of the that results or characteristic.

In contrast to applicant's assertions and as pointed out previously, Cummings et al. teach the use of PSGL in the treatment of acute and chronic conditions associated with leukocyte adherence, inflammation and <u>coagulation</u>, including <u>ischemia-reperfusion injury</u> and <u>atherosclerosis</u> (see column 18, paragraphs 5-8; columns 19-20). Cummings et al. teach the properties and the use of PSGL (column 9-18), including protein fragments thereof (e.g. column 20, paragraph 3) as well as the administration and monitoring according to one of ordinary skill in the art (column 21, paragraphs 2-3).

In addition with respect to "treating or inhibiting thrombosis", Cummings discloses that: Reperfusion injury is a major problem in clinical cardiology (columns 8-19, overlapping paragraph). Therapeutic agents that reduce leukocyte adherence in ischemic myocardium can significantly enhance the therapeutic efficacy of thrombolytic agents. Thrombolytic therapy with agents such as tissue plasminogen activator or streptokinase can relieve coronary artery obstruction in many patients with severe myocardial ischemia prior to irreversible myocardial cell death. However, many such patients still suffer myocardial necrosis despite restoration of blood flow. This reperfusion injury is know to be associated with adherence of leukocytes to vascular endothelium in the ischemic zone, presumably in part because of activation of platelets and endothelium by thrombin and cytokines makes they adhesive for leukocytes. These adherent leukocytes can migrate through the endothelium and destroy ischemic myocardium just as it is being rescued by restoration of blood flow."

Cummings further teach a number of clinical disorders associated with ischemia reperfusion (column 19, paragraph 1), coagulation (column 19, paragraph 2), and atherosclerosis (column 19, paragraph 6) that are associated with therapeutic endpoints, which include the inhibition of thrombosis as a therapeutic endpoint.

Treating cardiovascular diseases and disorders such as ischemia reperfusion injury and arteriosclerosis are consistent with applicant's disclosure on page 32 of the instant specification (Prophylactic and Therapeutic Methods).

Similarly, inhibiting platelet or leukocyte adhesion via P-selectin binding are the same desired endpoints disclosed by the instant specification (e.g. page 32 of the instant specification) and the prior art teachings of Cummings (see entire document, including Clinical Applications on columns 18-21)

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See <u>Bristol-Myers Squibb Company v. Ben Venue Laboratories</u> 58 USPQ2d 1508 (CAFC 2001).

Even though the claims include underlying mechanisms or physiology which contribute to thrombosis, the claims do not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

Cummings et al. also teach dosage ranges (e.g. 0.2 to 30 mg/kg body weight) for the treatment of inflammatory disorders (column 21, paragraph 1). Although this paragraph discloses carbohydrate inhibitors, the ordinary artisan would have immediately envisaged that this broad dosage range would have included other inhibitors (e.g. column 18, paragraph 4) as dictated by the specific condition (column 21, paragraphs 2-3). Also, given the nature of the acute and particularly the nature of chronic thrombotic conditions, one of ordinary skill at the time the invention was made would have provide the PSGL prior to thrombus formation.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed structural limitations (SEQ ID NO: 2 and P-selectin binding domains thereof) and the claimed functional limitations (e.g. inhibiting wherein the thrombus inducing agent is LTC<sub>4</sub>) would have been inherent properties of the referenced methods of treating various acute and chronic conditions associated with thrombosis with PSGL and fragments thereof and the properties of said PSGL and fragments thereof at the time the invention was made.

In addition, it is noted that applicant cites a study by Eppihimer and Schaub, Arterioslcer. Thromb. Vasc. Biol. 20 (11): 2483 - 2488 (2000) (1449) that shows the inhibition of thrombosis but not leukocyte adherence by recombinant PSGL-1.

However, Eppihimer does disclose the immunoneutralization of P-selectin with PSGL-1 does result in the reduction of thrombus formation (e.g., see Discussion), which is consistent with both the prior art teachings and the instant specification. Also, Eppihimer does disclose that it is possible that PSGL may inhibit leukocyte -platelet interactions and reduce the potential of thrombus formation by reducing the reactivity of leukocytes and platelets by reducing the reactivity of leukocyte and platelets to produce prothrombotic mediators (see Discussion), which is also consistent with the prior art teachings and the instant specification.

Applicant's arguments are not found persuasive.

23

5. Claims 1-5, 7-18 and 27-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Larsen et al. (U.S. Patent No. 5,840,679) (see entire document) for the reasons of record set forth in Paper No. 14.

Applicant's arguments, filed 5/28/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submit that Larsen fails to teach a method of treating or inhibiting thrombosis using PSGL-1 or teach that thrombosis is mediated specifically by P-selectin.

Applicant's arguments and the examiner's rebuttal are essentially the same as set forth above with respect to applicant's arguments against the teachings of Cummings.

Again, applicant is invited to note that the prior art teachings are directed to the same or nearly the same conditions as targeted by the instant specification (e.g. myocardial infarction), to the same or nearly the same mechanisms of action (e.g. inhibiting P-selectin mediated intercellular adhesion) as targeted by the instant specification) (e.g., compare columns 15-18 of Larsen with 25-26 of the instant specification).

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See <u>Bristol-Myers Squibb Company v. Ben Venue Laboratories</u> 58 USPQ2d 1508 (CAFC 2001).

Even though the claims include underlying mechanisms or physiology which contribute to thrombosis, the claims do not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

As pointed out in the last Office Action, Larsen et al. teach the use of PSGL (e.g.; columns 7-8, columns 13-18 and Examples), including fragments (e.g. columns 9-10) and fragments fused to carrier molecules such as immunoglobulins (e.g. chimeric forms of said PSGL (column 9-10, overlapping paragraph) to treat conditions characterized by P-selectin mediated intercellular adhesion, such as myocardial infarction (columns 15-16, overlapping paragraph), including its combination with other pharmaceutical compositions, including anti-inflammatory and thrombolytic or anti-thrombotic agents (e.g. columns 16-18) (see entire document, including Summary of the Invention; Detailed Description of the Invention). Larsen et al. also teach various modes of administration and dosing (e.g. liposomes, pharmaceutical carriers), including combinations of agents would be provided in therapeutically effective amounts either serially or simultaneously sufficient for the needs of the patient, including the nature and severity of the condition being treated according to the attending physician as well as doses ranges from about 0.1 ug to about 100 mg of isolated PSGL per kg body weight (columns 16-18). Larsen et al. teach soluble forms and fragments thereof which binds P-selectin comprising the same or nearly the same regions encompassed by the claimed human PSGL sequences (e.g. columns 9-15). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed structural limitations (SEQ ID NO: 2 and P-selectin binding domains thereof) and the claimed functional limitations (e.g. inhibiting wherein the thrombus inducing agent is LTC<sub>4</sub>) would have been inherent properties of the referenced methods of treating various conditions associated with thrombosis with PSGL and fragments thereof and the properties of said PSGL and fragments thereof at the time the invention was made

Applicant's arguments are not found persuasive.

6. Claims 1-20 and 23-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. patent No. 5,464,778) AND Larsen et al. (U.S. Patent No. 5,840,679) and in further evidence of Maugeri et al. (Thrombosis and Haemostasis 72: 450-456, 1994) for the reasons of record set forth in Paper No. 14.

Applicant's arguments, filed 5/28/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as addressed above with respect to the teachings of Cummings et al. and Larsen et al.

Applicant asserts that Maugeri is not pertinent to the instant claims.

Applicant acknowledges that Maugeri teaches the role of P-selectin in the synthesis of LTC<sub>4</sub> and that an anti-P-selectin antibody inhibited leukocyte-platelet interaction and reduced the synthesis of LTC<sub>4</sub>

However, applicant argues that Maugeri does not teach the PSGL-1 protein or its use for the inhibition of thrombosis.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. <u>In re Keller</u>, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. <u>In re Young</u> 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Applicant's arguments are not found persuasive.

Cummings et al. teach the use of PSGL in the treatment of leukocyte adherence, inflammation and coagulation, including ischemia-reperfusion injury and atherosclerosis (see column 18, paragraphs 5-8; columns 19-20, overlapping paragraph). Cummings et al. teach the properties and the use of PSGL (column 9-18), including protein fragments thereof (e.g. column 20, paragraph 3) as well as the administration and monitoring according to one of ordinary skill in the art (column 21, paragraphs 2-3). The claimed functional limitations would be expected properties of the referenced methods of treating atherosclerosis with PSGL and fragments thereof.

Cummings et al. differs from the claimed PSGL by not disclosing particular human PSGL sequences and domain structure thereof. Larsen et al. teach the structure, including the domain structure and the use of PSGL-derived fragments which are the same or nearly the same as that claimed (see columns 9-15).

Larsen et al. teach the use of PSGL (e.g.; columns 7-8, columns 13-18 and Examples), including fragments (e.g. columns 9-10) and fragments fused to carrier molecules such as immunoglobulins (e.g. chimeric forms of said PSGL (column 9-10, overlapping paragraph) to treat conditions characterized by Por E-selectin mediated intercellular adhesion, such as myocardial infarction (columns 15-16, overlapping paragraph), including its combination with other pharmaceutical compositions, including anti-inflammatory and thrombolytic or anti-thrombotic agents (e.g. columns 16-18) (see entire document, including Summary of the Invention; Detailed Description of the Invention).

Although Cummings et al. and Larsen et al. do not disclose all of the effective amounts recited in the instant claims 18-20, Cummings et al. and Larsen et al. teach the art known provision effective amounts of PSGL which inhibit P-selectin binding to treat thrombotic conditions to meet the severity of the condition and the needs of the patients. Therefore, the modes of administration and dosages encompassed by the claimed invention (claims 17-20) would have been met by the ordinary artisan at the time the invention was made to meet the severity of the conditions and the needs of the patients. For example, Larsen et al. also teach various modes of administration and dosing (e.g. pharmaceutical carriers), including combinations of agents would be provided in therapeutically effective amounts either serially or simultaneously sufficient for the needs of the patient, including the nature and severity of the condition being treated according to the attending physician (columns 16-18).

Although Cummings et al. and Larsen et al. do not disclose the role of  $LTC_4$  in thrombus formation and thrombotic conditions per se,  $LTC_4$  was a known thrombus-inducing agent in thrombus formation and thrombotic conditions. Therefore, one of ordinary skill in the art would have expected that the methods of treating thrombotic conditions taught by Cummings et al. and Larsen et al. would have inhibited the thrombus inducing agent in a subject, including  $LTC_4$  at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to administer PSGL-1, fragments and chimeric constructs thereof, provided they had the properties of inhibiting PSGL-1-mediated interactions and inflammatory responses, as taught by Cummings et al. and Larsen et al. to treat patients with various thrombotic conditions. Given the teachings of Cummings et al. and Larsen et al. to inhibit PSGL-1-mediated interactions and inflammatory responses, including those associated with coronary/thrombotic conditions, the ordinary artisan would have had a reasonable expectation of success at the time the invention was made to treat or inhibit thrombosis, to increase the movement of cells relative to blood vessels and to inhibit the effect of thrombus-inducing agents, as properties of such treatment of PSGL-1-mediated interactions and inflammatory responses. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claims 25-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. patent No. 5,464,778) AND Larsen et al. (U.S. Patent No. 5,840,679) as applied to claims 1-20 and 23-27 above and in further evidence of Maugeri et al. (Thrombosis and Haemostasis 72: 450-456, 1994) and Johnston et al. (J. Immunol. 159: 4514-4523, 1997) for the reasons of record set forth in Paper No. 14.

Applicant's arguments, filed 5/28/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as addressed above with respect to the teachings of Cummings et al., Larsen et al. and Maugeri et al.

Applicant acknowledges that Johnston et al. teach the role of LTC<sub>4</sub> in leukocyte adhesion and the ability of anti-P-selectin antibody to inhibited leukocyte adhesion. Applicant's argue that Johnston et al. does not teach PSGL-1 or its ability to inhibit thrombosis.

Again, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Again, although Cummings et al. and Larsen et al. do not disclose the role of  $LTC_4$  in thrombus formation and thrombotic conditions per se,  $LTC_4$  was a known thrombus-inducing agent in thrombus formation and thrombotic conditions, as evidenced by Maugeri et al. and Johnston et al.. Therefore, one of ordinary skill in the art would have expected that the methods of treating thrombotic conditions taught by Cummings et al. and Larsen et al. would have inhibited the thrombus inducing agent in a subject, including  $LTC_4$  at the time the invention was made. Further, both Maugeri et al. And Johnston et al. teach that inhibiting P-selectin-mediated events results in the inhibition of thrombus-inducing biological substances, including  $LTC_4$ .

One of ordinary skill in the art at the time the invention was made would have been motivated to administer PSGL-1, fragments and chimeric constructs thereof, provided they had the properties of inhibiting PSGL-1-mediated interactions and inflammatory responses, as taught by Cummings et al. and Larsen et al. to treat patients with various thrombotic conditions. Given the teachings of Cummings et al. and Larsen et al. to inhibit PSGL-1-mediated interactions and inflammatory responses, including those associated with coronary/thrombotic conditions, the ordinary artisan would have had a reasonable expectation of success at the time the invention was made to treat or inhibit and to inhibit the effect of thrombus-inducing agents, as properties of such treatment of PSGL-1-mediated interactions and inflammatory responses. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

- 8. No claim is allowed.
- 9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD. Primary Examiner

PECUP GIMENE

Technology Center 1600

July 28, 2003